1196-17 The Impact of Intracoronary Radiation on In-Stent Restenosis Involving Ostial Lesions

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Background: Coronary interventions in ostial lesions have a high rate of recurrence of restenosis. The aim of this study was to compare 6-month clinical and angiographic outcomes of patients (pts) with in-stent restenosis (ISR) involving the ostium treated with intra-coronary radiation therapy (IRT) compared to placebo and also to non-ostial lesions treated with IRT. **Methods:** We assessed 1295 pts enrolled in gamma (192-Iridium) and beta (90-Yttrium) radiation trials for ISR at the Washington Hospital Center. Of pts receiving IRT, 99 (8%) pts had ostial ISR and 1169 (90%) pts had non-ostial ISR, and only 27 pts had ostial ISR and were treated with placebo. **Results:** Baseline demographic, angiographic and procedural details were similar, except ostial IRT pts had a trend towards shorter lesions (14.0±10.8 vs. 32.4±14.3 mm, p=0.06), and had a higher rate of saphenous vein graft disease (47% vs. 19%, p<0.001), compared to non-ostial IRT pts. Ostial lesions treated with IRT for ISR had a reduced rate of recurrent restenosis compared to ostial lesions treated with placebo (Table). Outcomes at 6 months including restenosis rates were similar for the ostial and non-ostial IRT group. **Conclusions:** Intracoronary radiation continues to be effective for ostial in-stent restenotic lesions and should be comfortably used for this challenging anatomic location.

Clinical and Angiographic Outcomes at 6 Months

	IRT		Placebo
	Ostial (N=99)	Non-Ostial (N=1169)	Ostial (N=27)
Angiographic Restenosis, %	11	29*	55†
Late Loss, mm	0.33±0.70	0.47±0.72	0.99±0.64†
TVR, %	23	22	50†
MACE, %	25	22	54†
Late Total Occlusion, %	2	4	4

*P < 0.05 IRT Ostial vs. IRT Non-Ostial,
†P < 0.05 IRT Ostial vs. Placebo Ostial

1196-18 High Dose Intracoronary Gamma Radiation for Patients With Diffuse In-Stent Restenosis: Six Versus One Month of Antiplatelet Therapy

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Background: The Washington Radiation for In-Stent Restenosis Trial for long lesions, utilizing high dose (18 Gy) of intracoronary radiation therapy (IRT): LONG WRIST HIGH DOSE, aimed to determine the safety and efficacy of higher doses of γ IRT for the treatment of patients (pts) with diffuse in-stent restenosis (ISR). **Methods:** One hundred and twenty pts with diffuse ISR in native coronary arteries (lesion length 36-80 mm) underwent PTCA, atherectomy, and/or additional stents. The prescribed dose was 18 Gy at 2.0 mm, with a mean ribbon length of 69 ± 6 mm. Six month (mo) clinical outcomes of 60 pts treated with 1 mo of Clopidogrel were compared to 60 pts with 6 mos of Clopidogrel. Additional comparison was made to pts from LONG WRIST who were randomized to placebo (n=61) or 192-Ir with a prescribed dose of 15 Gy at 2 mm (n=60) with 1 mo of Ticlopidine. **Results:** All 120 pts treated with 18 Gy underwent successful IRT. The overall events at 6 mos were lower in the high dose group compared to pts treated with 15 Gy or placebo (Table). Six mos of antiplatelet therapy (APT) in the high dose group was associated with less thrombotic events when compared to one mo of APT. **Conclusions:** High dose radiation (18 Gy) using 192-Ir for diffuse ISR is safe and effective (compared to control and a dose of 15 Gy). Prolonged antiplatelet therapy continues to be protective for late thrombosis even in higher doses of radiation.

	18Gy 1M APT (N=60)	18Gy 6M APT (N=60)	15Gy 1M APT (N=60)	Placebo 1M APT (N=61)	P
Death, %	0	0	5	2	0.11
Q-Wave MI, %	0	5	5	0	0.10
TLR, %	18	14	30	57	<0.001
TVR, %	28	17	33	57	<0.001
MACE, %	28	16	37	59	<0.001
Late Thrombosis, %	8	2	10	5	0.20

1196-19 Prolonged Antiplatelet Therapy and Reduced Stenting Eliminates Late Thrombosis After Radiation: The Scripps III Trial

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Background: While the efficacy of coronary brachytherapy for the treatment of in-stent restenosis has been well established, recent reports of excess late thrombosis, leading to myocardial infarction, have raised safety concerns. Previous studies have linked thrombotic episodes to new stent implantation and early discontinuation of antiplatelet therapy. The objective of the SCRIPPS III study was to evaluate the impact of both reduced additional stent implantation and enhanced adjunctive antiplatelet therapy on late target thombosis following brachytherapy.
Methods: At two centers (Scripps Clinic and Lenox Hill) vigorous attempts were made to avoid implanting new stents prior to treatment of in-stent restenosis with gamma radiation. Patients who did not receive new stents were discharged on clopidogrel (75mg per day after a 300mg loading dose) for 6 months and patients who received new stents were treated with clopidogrel for 12 months. All patients received aspirin, 325mg, indefinitely.
Results: Enrollment in this 500 patient registry was completed on 9/12/00; 33.8% had diabetes, 15.2% had treatment of a saphenous vein graft and 39% were treated with a radiation source wire ≥ 55mm in length. New stents were implanted in only 22.7% of study patients. The mean current follow-up time is 11.1 months. Clopidogrel has been discontinued for more than 1 month in 243 (48.6%)patients. To date, one patient who received a new stent sustained an acute stent thrombosis six hours after the index radiation procedure due to distal dissection and two patients who received a new stent sustained a stent thrombosis within two weeks following radiation. There have been no late (≥ 30 day) thromboses.
Conclusion: Minimizing new stent implantation and treatment with prolonged adjunctive antiplatelet therapy appears to eliminate late target thrombosis after coronary brachytherapy. Final follow-up results will be presented.

1196-20 Interprocedural Interval as a Risk Factor for Recurrent Restenosis After Treatment of In-Stent Restenosis: Differential Response With and Without Brachytherapy

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In patients undergoing reintervention for in-stent restenosis, a short interval (<90 days) between index and repeat procedures has been identified as an important risk factor associated with recurrent restenosis. We hypothesized that brachytherapy (due to its effects on actively dividing cells) would have greater benefit in patients with short interprocedural intervals and would minimize the importance of the temporal interval as a predictive factor for restenosis. In this START substudy, the effect of beta-radiation vs placebo for the treatment of in-stent restenosis was assessed as a function of the interval between procedures. Compared to patients with intervals >90 d, patients with early restenosis (≤90 d) had smaller vessels (2.66 vs 2.83 mm, p<.05) and were more likely to have class III/IV angina (71 vs 50%, p=.01). Multivariable modeling for recurrent in-stent restenosis demonstrated a significant interaction between the interprocedural interval and restenosis; patients with a prior procedure ≤90 d had higher restenosis risk (odds ratio 5.58, p=.001). Multivariable modeling also demonstrated a significant benefit associated with Sr90 therapy (odds ratio 0.42, p<.05). An interaction between assigned therapy and interprocedural interval was observed. The relation between the interval and restenosis was different for Sr90 vs placebo in that radiation markedly reduced the time effect. For Sr90 patients, recurrent restenosis was comparably low in both early and late groups (11.8 vs 13.6%). In contrast, placebo patients with early repeat procedures were at higher risk of restenosis (66.7 vs 26.4%). Thus, the relative treatment effect of radiation was greater in the early procedure group than in the late group (82 vs 48% reduction).
Conclusions: (1) Risk of in-stent restenosis is inversely related to the interprocedural interval - patients with restenosis within 90 days have higher risk of recurrent restenosis; (2) The relative effect of b-radiation is greater in patients undergoing early repeat procedures but the absolute restenosis rates are low irrespective of the interprocedural interval; (3) Brachytherapy eliminates the effect of the temporal interval on recurrent restenosis.

1196-21 Retreatment Immediately After Gamma Radiation for In-Stent Restenosis Results in Need for Target Vessel Revascularization Beyond Target Lesion

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Background: Repeat balloon angioplasty or stenting (re-treatment) immediately after gamma radiation for in-stent restenosis (ISR) is sometimes required, usually due to acute recoil. However, little is known about short and long-term outcomes after re-treatment following brachytherapy.
Methods: Balloon angioplasty plus gamma radiation was performed in 154 ISR lesions. Re-treatment after brachytherapy was required in 48 lesions (31%).
Results: Baseline clinical characteristics were similar between the 2 groups. There were no late thromboses. In the subset of lesions with no new stents, TVR (target vessel

revascularization) without TLR (target lesion revascularization) was higher in those with re-treatment compared to no re-treatment (19.2% vs. 3.4%, p=0.02).
Conclusions: Re-treatment after gamma radiation is performed in one-third cases, often resulting in additional stent implantation. Re-treatment is associated with increased TVR at follow-up, probably due to injury outside the irradiated segment. If re-treatment is required, vigorous efforts to avoid injury to inadequately irradiated vessel segments and additional stenting should be made.

	No re-treatment	Re-treatment	p Value
New stents (%)	12	42	<0.01
Reference diam (mm)	2.84±0.45	2.86±0.40	0.8
Lesion length (mm)	18.1±8.6	20.1±9.1	0.2
Pre-MLD (mm)	0.60±0.44	0.58±0.42	0.8
Final MLD (mm)	2.69±0.53	2.68±0.52	0.9
In-hosp MACE (%)	0	2.1	0.3
9-month MACE (%)	13.1	11.1	1.0
9-month death (%)	2.1	0	1.0
9-month MI (%)	2.1	8.9	0.08
9-month TVR (%)	12.1	22.2	0.14
9-month TLR (%)	10.1	6.7	0.8
9-month TVR without TLR (%)	3.1	17.8	<0.01

1196-22 Efficacy of Gamma Vascular Brachytherapy for Ostial Versus Nonostial In Stent Restenotic Lesions

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Background: In stent restenosis (ISR) involving the coronary ostium is associated with high recurrence rates after conventional treatment compared to non-ostial lesions. Whether Gamma vascular brachytherapy (GVBT) significantly improves these outcomes is not known. Methods: Pts with native ostial coronary lesions (N=45) were selected from a pooled angiographic database of pts enrolled in Vascular Brachytherapy (VBT)trials for treatment of ISR and were compared to 232 pts with non-ostial lesions, matched for lesion length. Baseline and follow-up quantitative coronary angiographic (QCA) analysis were assessed and compared. Results: At baseline pts with ostial lesions had more complex lesions (ACC/AHA > B1: 73.3% vs. 53.8%, p<0.05), with more total occlusions (8.9% vs. 3.0%, p=0.08) compared to non-ostial pts. QCA results are presented in the table.
Patients with VBT failure had a significant reduction in lesion length regardless the lesion location: ostial (14.2±9.49 to 6.94±3.69,p<0.05) and non-ostial (16.66±6.71 to 8.61±6.52, p<0.005).There were no difference in stent edge restenosis (6.7% vs. 9.1%,p=0.77) Conclusions: Gamma radiation is at least as effective for treatment of ostial in-stent restenotic lesions as non-ostial lesions, decreasing restenosis by 54% compared to non-ostial lesions. The difference was not related to edge restenosis.

QCA analysis	Ostial	Non-Ostial	p Value
Lesion length Pre(mm)	14.2±9.4	16.6±6.7	0.25
Lesion length FU(mm)	6.9±3.6	8.6±6.5	0.07
Reference (mm)	2.71±0.39	2.61±0.46	0.15
Final DS%	26.9±14.5	27.8±12.2	0.67
FU DS%	36.8±21.7	47.2±25.1	0.009
Late Loss (mm)	0.31±0.58	0.52±0.70	0.05
Restenosis (%)	17.8	32.8	0.04

1196-23 Repeat Intracoronary Radiation for In-Stent Restenosis in Patients Who Failed Radiation Therapy: Re-WRIST

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Background: Intracoronary Radiation (IR) is proven as an effective therapy to prevent recurrences of in-stent restenosis (ISR). However nearly 20% of the patients (pts) enrolled in radiation studies for ISR required repeat revascularization to the irradiated site. Re-WRIST (Washington Radiation for In-Stent Restenosis Trial) is a registry evaluating the safety and efficacy of re-treatment with IR in pts with refractory ISR.
Methods: Patients with ISR who had recurrence of stenosis at a previously irradiated segment and failed a subsequent additional angioplasty were eligible for re-treatment with IR, if evaluated as a poor surgical candidate. In Re-WRIST, the radiation system is a 0.0030-inch nylon ribbon containing 192Ir seeds manufactured by Best Industries delivered into a non-centered end lumen delivery catheter (Cordis 4F or Medtronic 5F). The prescribed dose is 15 Gy to a 2 mm radial distance from the center of the source. All pts receive 6 months of clopidogrel post-procedure. Patients are followed clinically, angiographically and by IVUS at 6 and 24 months.
Results: At present, 9 pts have been enrolled in the Re-WRIST registry. The mean age of the cohort is 65 ± 10yrs (4 males, 3 diabetics and 7 pts had previous CABG). Five ISR lesions were in native coronary arteries, 3 in saphenous vein grafts and one in left internal mammary artery. The mean time interval between radiation treatments is 18 months (range 6.4-28.9) and the mean number of previous interventions to the target lesion is 4.1 ± 1.5. The radiation was delivered successfully in all pts with no procedural or hospital complications. Balloon angioplasty alone was performed in 6 of 9 pts, 2 pts were treated with the excimer laser and 1 pt with the cutting balloon. None of the pts received additional stents. At 30 days, there were no reported clinical events.
Conclusions: Repeat radiation to the same site using 192-Ir for refractory ISR is safe and effective at 30 days. Complete 6-month clinical and angiographic follow-up will be available at presentation.

1196-24 Age is an Important Predictor of Clinical Outcomes Following Intracoronary Radiation Therapy for In-Stent Restenosis

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Background: Intracoronary radiation therapy (IRT) reduces the recurrence rate of in-stent restenosis (ISR) by inhibition of smooth muscle cell proliferation. The ability of these cells to replicate is limited with age due to changes in the telomeres. The purpose of this study was to assess the effect of age on clinical outcomes following IRT for ISR.
Methods: We evaluated 1275 patients (pts) with 6-month (mo) clinical follow-up who were enrolled in radiation trials for ISR using gamma and beta emitters conducted at the Washington Hospital Center. Patients with ISR who were assigned to IRT (N=1025) or placebo (N=250) were analyzed in 4 age groups: (<55 yrs, 55-64 yrs, 65-75 yrs, >75 yrs).
Results: Baseline clinical and angiographic characteristics were similar within each age group of IRT pts, except for a higher rate of diabetes in younger pts (42% in pts <75 yrs vs. 30% in pts >75 yrs, p=0.002) and a higher rate of previous CABG in older pts (58% in pts >75 yrs vs. 37% in pts <55 yrs, p< 0.001). The clinical outcomes at 6 mos for IRT treated pts are shown (Table). No effect of age was seen in placebo pts. IRT treated pts had reduced MACE compared to placebo in all age groups, driven by reduced target vessel revascularization (TVR). Multivariate analysis detected age as an independent predictor of MACE at 6 mths (odds ratio 0.8, CI. 0.70-0.93, p=0.004). **Conclusions:** Elderly pts (>75 yrs) potentially derive the maximum benefit from IRT for ISR as recurrent restenosis is significantly reduced compared to younger pts.

	< 55 yrs (N=268)	55-64 yrs (N=321)	65-75 yrs (N=314)	>75 yrs (N=122)	P
Death, %	1	3	4	4	NS
Q-Wave-MI, %	2	1	1	1	NS
TLR, %	19	21	13	8	0.002
TVR, %	28	26	19	16	0.005
MACE, %	28	28	20	18	0.02
Late Thrombosis, %	3	2	1	1	NS

POSTER SESSION

1197 Carotid Interventions II

Tuesday, March 19, 2002, 3:00 p.m.-5:00 p.m.
Georgia World Congress Center, Hall G
Presentation Hour: 3:00 p.m.-4:00 p.m.

1197-6 Neuroprotection Reduces the Risk of Peri-Procedural Major Strokes and Death in Octogenarians

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Background: Our previous work in carotid stenting (CS) suggested that patients ≥ 80 years of age compared with those < 80 are higher- risk for procedural related stroke. Since then, we have altered our strategy of performing CS in ≥ 80 years under neuroprotection (NP). The aim of this study was to compare procedural outcomes in patients ≥ 80 years with and without distal embolic protection.
Methods: Thirty- day outcomes (TIA, minor strokes, major strokes and myocardial infarction) were prospectively examined in those patients ≥ 80 years of age who had undergone CS with and without NP.
Results: There were no differences in age, % female, presence of risk factors, CAD, contralateral occlusion, and procedural success between the two groups. There were more patients in the NP group who were asymptomatic (64% vs. 44%), and with prior carotid endarterectomy (23% vs. 10%).

30 Day Outcomes	Without NP	With NP
Patient	91	47
Minor Stroke	7 (7.7%)	3 (6.4%)
Major Stroke	6 (6.6%)	0
Fatal Stroke	1 (1.1%)	0
Non- Stroke Death	1 (1.1%)	1 (2.1%)
Total	15 (16%)	4 (8.5%)

*P= 0.06